plant oils and animal fats were probably the base materials to which more expensive ingredients (resins, for example, some of which may have been imported from Lebanon) were added.

The authors point out that the amount of coniferous resins and beeswax increases in later mummies, implying that these substances became more important with time. They also stress the variety and compositional diversity of embalming materials. This finding is consistent with what other researchers have found: embalming materials and procedures vary more than expected, both within single dynasties and between historical periods[10]. This could be a result of economics (the cost and availability of materials), changing fashions, and/or the preferences of particular embalming guilds.

Buckley and Evershed tested 13 mummies of known provenance and date spanning approximately 2,300 years. However, only one or two mummies from each dynasty or period are represented (except for the Roman period, 30 BC to AD 395, for which four mummies were tested). Larger numbers of mummies from each period need to be analysed before we can conclude, for example, that Egyptian embalmers never used bitumen from the Dead Sea , or that bitumen was used only during the Roman period. (If this substance was used exclusively during Roman times, perhaps the reason was that it was cheaper or easier to transport under Roman rule.) Ideally, these mummies should be selected from those of known provenance and date to provide maximum information, but this is by no means easy — many mummies now residing in museums around the world are woefully deficient in documentation. In some cases, such as Roman mummies that can be dated fairly precisely by the style of the accompanying portraits, chemical analysis could contribute to our knowledge about embalming practices during a particular period without knowing the specific site of the mummy's origin.

As more mummies are tested, a larger database of embalming substances from all periods will help archaeologists explain variation in terms of changing economics and customs, as well as knowledge of material properties. For example, a preference for scented cedar oil over juniper oil in a particular period might indicate a choice based on fashion and cost, rather than preservative properties. The two coniferous oils are similar, but juniper oil was presumably cheaper to import from Lebanon because juniper was a more common tree than cedar. Wealthy Egyptians may have deliberately chosen the more expensive embalming fluid to impress family and friends, just as well-to-do people today select exotic woods and metal trims for their relatives' coffins. ■

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Molecular dynamics

Slick switching of X-rays

Ferenc Krausz and Christian Spielmann

The structures of crystals, from metals to proteins, have successfully been explored with X-rays. An ultrafast switch turns this idea around and uses a crystal to control the timing of X-ray pulses.

Since their discovery some 100 years ago by Wilhelm Röntgen[1], X-rays have found important uses in hospitals, laboratories and the exploration of space. They have proved particularly useful in investigations of the microscopic structure of matter[2]. By scattering X-rays from small molecules, large biopolymers or macroscopic crystals, scientists can determine how the constituent atoms are arranged relative to each other. But obtaining fundamental information about the dynamics of molecular reactions is much harder, as it requires the motion of constituent atoms to be followed over interatomic distances. To achieve this, the X-rays must be switched on and off within a time period short enough to 'freeze' atomic motion. This is an enormous challenge.

On page 825 of this issue, DeCamp *et al.*[3] show how to control the proportion of X-rays transmitted through a crystal on a picosecond timescale (1 picosecond is 10^{-12} s). With this method it may be possible to develop a sub-picosecond X-ray switch, which would be fast enough to track dynamic changes in molecular structure during chemical and biochemical reactions.

Traditional X-ray structural analysis, although it cannot follow the progression of reactions, provides insight into how molecules work, and so is a key experimental technique for the chemical and life sciences.

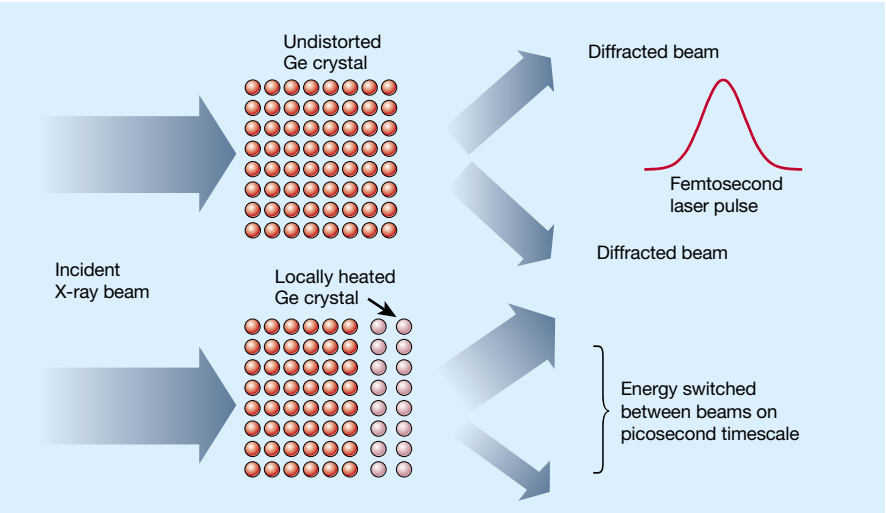

Figure 1 **Blink and you'll miss it. An ultrafast switch for X-rays has been created by DeCamp *et al.*[3] with the goal of generating ultrashort X-ray pulses that can track molecular dynamics during chemical and biochemical reactions. The switch is based on a germanium crystal that transmits X-rays with high efficiency (owing to the Borrmann effect). When the X-ray beam leaves the crystal it splits into two diffracted beams with roughly equal intensities. The structure of the crystal can be modified on a femtosecond timescale by using a laser pulse to heat and expand the lattice. The X-ray transmission is extremely sensitive to small lattice distortions, allowing the intensities of the diffracted beams to be modified on ultrafast (pico- to femtosecond) timescales, and even switched on and off, generating ultrashort pulses.**

The equilibrium positions of atoms in complex molecules can be measured with a breathtaking accuracy of 10^{-13} m (about one-thousandth of a molecular bond length). Knowing the equilibrium structure of molecules allows physicists and chemists to predict how they might behave in different situations, but definite answers to many important questions require the direct observation of molecular dynamics.

Molecular processes, such as the breaking or formation of chemical bonds, have already been investigated by ultrafast pump-probe experiments, which use an intense femtosecond (10^{-15} s) laser pulse to trigger a reaction and a weak time-delayed probe pulse (operating at visible or longer wavelengths) to take snapshots of the subsequent dynamics[4]. But in these studies it is possible to follow changes in the atomic positions of only the simplest molecules. This is because the visible light can only probe the optical properties of weakly bound atomic electrons, from which the atomic positions can be inferred for simple molecules only. By contrast, 'hard' X-rays with wavelengths 5,000 times smaller than visible light can be absorbed or scattered by strongly bound 'core' electrons, providing direct information about the positions of the nuclei. So variation in the absorption or diffraction of hard X-rays can be unambiguously related to dynamic changes in molecular structure regardless of its complexity.

These prospects triggered a worldwide effort to develop sources of ultrashort pulses of hard X-rays. One successful approach has been to strip electrons from atoms (forming a plasma of ions and electrons) and then accelerate the electrons to velocities close to the speed of light using a powerful femtosecond laser pulse. When the energetic electrons re-collide with the atomic cores they produce a short X-ray burst at wavelengths characteristic of the atoms in the target. Such laser-driven sources of hard X-rays have already been used in proof-of-principle demonstrations of ultrafast X-ray absorption and diffraction measurements[5–7].

Hard X-rays can also be created in a particle accelerator known as a synchrotron without the need for any collisions. Synchrotron radiation is emitted by high-speed electrons following a circular path through a strong magnetic field, and delivers pulses typically tens of picoseconds in duration. Last year, physicists produced sub-picosecond bursts of hard X-rays in a synchrotron for the first time by manipulating the electrons radiating the X-rays with a powerful femtosecond laser[8].

The work of DeCamp *et al.*[3] opens an entirely new chapter in controlling the time structure of hard X-rays. The authors modified the transmission of a synchrotron X-ray beam through a germanium crystal on a picosecond timescale by stimulating changes in the crystal lattice with an ultrashort laser pulse. This X-ray 'switch' allows them to modulate hard X-ray beams regardless of their source of emission, and thereby turn the X-rays on and off to generate sequences of pulses, or even shaped pulses, over a wide range of hard-X-ray wavelengths.

The prototype X-ray switch developed by DeCamp *et al.* consists of a thin piece of germanium crystal irradiated by strong femtosecond laser light. By cutting and aligning the crystal in the correct way the authors have created an unusually high transmittivity for the incident hard X-rays. At the exit face of the crystal the transmitted X-ray beam is split into two diffracted beams, which propagate with nearly equal intensities in slightly different directions (Fig. 1). The relative transmittivity and intensity of the two X-ray beams is sensitive to minor distortions in the crystal structure. The exit face of the crystal can be heated up quickly with a femtosecond laser pulse; the heated volume expands, shifting atoms out of their equilibrium position in the lattice (by a process known as acoustic phonon excitation). So the structure of the lattice is perturbed, modifying the transmission of the incident X-ray beam and redistributing energy between the two outgoing X-ray beams. In this way the beams can be switched on and off, or the relative strengths of the two beams can be quickly altered.

When the X-ray switch is in operation the crystal atoms move only a fraction away from their equilibrium position, but this is still sufficient to switch a substantial fraction of X-ray energy from one beam to the other. This experiment beautifully demonstrates the sensitivity of X-ray diffraction to atomic positions, a feature that X-ray structural analysis itself relies upon. The X-ray energy flow into the outgoing diffracted beams is switched within the time it takes the atoms to leave their equilibrium position. This limits the minimum switching time to picoseconds in the current experiment, but the transmission of the X-ray beam can also be affected by small perturbations in the distribution of electrons around the atoms in the crystal lattice. Because electrons are much lighter than the nuclei forming the lattice, such perturbations (referred to as optical phonons) could be generated on a much faster sub-picosecond timescale with a sufficiently short laser pulse. Using electronic instead of acoustic perturbations could bring the switching time down to less than a picosecond, paving the way to eventually creating hard X-ray pulses of femtosecond duration.

How does this method compare with other techniques used to control X-rays on an ultrafast timescale? Laser-driven hard X-ray sources can generate pulses that are shorter than a picosecond but, because they emit photons in all directions, only a fraction of the X-ray photons can be focused on the

100 YEARS AGO

Paris was greatly excited on Saturday last when M. Santos Dumont, with his seventh balloon, successfully rounded the Eiffel Tower and returned to the shed at St. Cloud, thirty seconds within the thirty minutes allotted by the Committee of the Deutsch Prize. At the time of the voyage the wind, according to the *Times* correspondent, was blowing at the rate of twelve of thirteen miles an hour. At one period the balloon, travelling at the rate of thirty miles an hour, appeared as though it would collide with the Tower; the aeronaut, however, was able to control its movements without any apparent difficulty, and, as has been said, the journey was accomplished within the time limit agreed upon. M. Santos Dumont is to be congratulated upon the success which has at last attended the untiring efforts put forward by him towards the solution of the problem of aerial navigation.

From *Nature* 24 October 1901.

50 YEARS AGO

The second International Congress on Astronautics was held in London during September 3–8. It was attended by nearly fifty delegates representing societies and groups interested in astronautics from Argentina, Austria, France, Germany, Great Britain, Italy, Spain, Sweden, Switzerland and the United States… The latter part of the London Congress was devoted to a symposium of papers on the general theme of orbital vehicles, their construction and uses. There was general agreement among the speakers that such vehicles are possible from an engineering point of view; the first instrument-carrying vehicles could be built within ten to fifteen years; but man-carrying artificial satellites appear to be much further in the future… The greatest problem of interplanetary flight is that of propulsion, and in his paper "Interplanetary Travel between Satellite Orbits", Prof. Lyman Spitzer discussed a method of applying nuclear energy. It was suggested that an electrically accelerated ion beam could be used for achieving a gas ejection velocity of 100 km./sec. without the use of very high temperatures in the propellant gases. Such a unit could not be built with a large enough thrust/weight ratio to allow it to take off from the surface of a planet. It would be capable of travelling from a close-orbital station about the earth to a similar orbit about any other planet.

From *Nature* 27 October 1951.

material of interest. Synchrotrons are able to produce strong, collimated (laser-like) beams of hard X-rays, exposing targets to many more photons, but techniques that shape the electron beam in a synchrotron to generate ultrashort pulses require expensive modifications to the X-ray source. This is feasible only for dedicated beam lines. By contrast, DeCamp and colleagues' X-ray switch is a versatile tool that could be added to nearly every beam line without having to touch the source. Many challenges remain, such as shortening the switching time by using electronic excitations, and improving the switching efficiency to produce X-ray pulses with good contrast. But once these problems have been solved, such ultrafast switches could become a key component in the X-ray toolbox for probing the structural dynamics of matter. ■

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Developmental biology

Solving a sticky problem

Christof Niehrs

The Wnt family of proteins is a large one. Various combinations of its members control all sorts of developmental processes, including, it now seems, a pathway involving cell adhesion.

In this age of the genome, molecular biologists are often told that, to stay competitive, they must use genomics and *in silico* techniques when studying protein function. Well, here is a riddle for advocates of this approach. Proteins in the Wnt family are involved in cell-to-cell signalling during nearly every process one can think of in animal development, from the formation of the embryonic axes to kidney development, and from invertebrates to humans. In humans alone there are at least 19 genes encoding Wnt proteins, and ten receptors for these proteins.

So, how do you investigate the specificity of biological responses to Wnts? The answer, according to Winklbauer *et al.* (page 856 of this issue[1]), is to use a cell-biological approach and — even more disturbingly — old-fashioned amphibian embryos. In this way the authors provide good evidence that vertebrates have three signalling cascades triggered by Wnts, which separately regulate cell differentiation, cell polarity and cell adhesion.

The best-characterized signalling cascade triggered by Wnt proteins is the canonical, or Wnt/β-catenin, pathway (Fig. 1a). Details of this cascade first emerged from genetic analyses of fruitflies (*Drosophila*), where it functions in developmental processes such as the patterning of body segments and appendages. Since then we have learned, through work in vertebrates as well, that the canonical pathway is actually a large network. At its heart is the multifunctional protein β-catenin, most of which is bound to the internal face of the plasma membrane. In the absence of signalling from Wnt, a large molecular complex ensures that β-catenin is rapidly targeted to the cellular protein-degrading apparatus. Activation of the pathway by a Wnt protein results in β-catenin being stabilized; it then enters the nucleus, where, with proteins of the high-mobility-group family, it activates the expression of specific genes to control cell fate[2].

The existence of the planar cell polarity (PCP) pathway was also revealed by genetic analysis of *Drosophila*[3]. Cuticle cells in adult fruitflies secrete hairs, which are polarized by the PCP pathway so that they all point in one direction. The PCP pathway is also at work in vertebrates during gastrulation — the massive rearrangement of cells that produces the three main tissue layers, endoderm, mesoderm and epidermis, in the early embryo. During gastrulation, migrating cells become polarized by the PCP pathway and extrude lamellipodia — extensions that help movement — along one axis only[4]. The common theme to both processes is the polarization of the cytoskeleton.

In *Drosophila*, the receptor protein that lies at the start of the PCP signalling pathway is Frizzled. It is not known how this receptor is switched on in the fruitfly — that is, which protein binds to it to activate the pathway. But the vertebrate PCP pathway is triggered by Wnt11 (refs 5, 6; Fig. 1b), so a Wnt protein may well be involved in the *Drosophila* pathway, too. Instead of using β-catenin, the PCP pathway works through small GTP-binding proteins from the Cdc42/Rho family, which activate the transcription factor Jun.

Hints that there might be a third Wnt-triggered pathway came from the discovery[7–9] that Wnt5a, together with another member of the Frizzled family, Frizzled-2, mobilizes Ca^{2+} ions within cells and thereby activates certain Ca^{2+}-dependent enzymes,

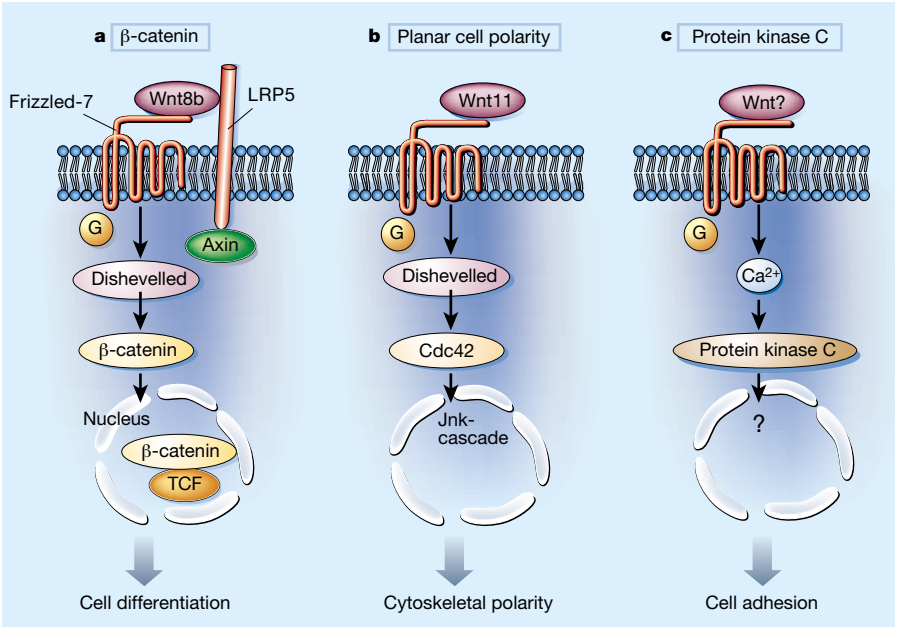

Figure 1 **Three signalling cascades that are triggered by Wnt proteins in vertebrates. The choice of pathway activated by the Wnt receptor Frizzled-7 depends on which particular Wnt protein is outside the cell.** a, **Wnt8b triggers the β-catenin cascade[10,11]; it achieves specificity by using a co-receptor, LRP5, which itself controls Axin[13], a negative regulator of β-catenin.** b, **Wnt11 activates the planar cell polarity pathway[4–6,12].** c, **An unknown Wnt works through Frizzled-7 to induce an increase in the Ca^{2+} level inside cells and thereby activate protein kinase C[1,7–9]. All three pathways also use molecular adaptors known as heterotrimeric G proteins (represented by G).**